CLAIMS

1. An isolated and purified huBUB3 protein having an amino acid sequence which is at least 85% identical to SEQ ID NO:2, wherein percent identity is determined using a Smith-Waterman homology search algorithm using an affine gap search with a gap open penalty of 12 and a gap extension penalty of 1.

2. The isolated and purified huBUB3 protein of claim 1 which has the amino acid sequence shown in SEQ ID NO:2.

3. An isolated and purified polypeptide comprising at least 8 contiguous amino acids as shown in SEQ ID NO:2.

4. A huBUB3 fusion protein comprising a first protein segment and a second protein segment fused together by means of a peptide bond, wherein the first protein segment consists of at least 8 contiguous amino acids of a huBUB3 protein as shown in SEQ ID NO:2.

5. A preparation of antibodies which specifically bind to a huBUB3 protein having an amino acid sequence as shown in SEQ ID NO:2.

6. A cDNA molecule which encodes a huBUB3 protein having an amino acid sequence which is at least 85% identical to SEQ ID NO:2, wherein percent identity is determined using a Smith-Waterman homology search algorithm using an affine gap search with a gap open penalty of 12 and a gap extension penalty of 1.

7. A cDNA molecule which encodes at least 8 contiguous amino acids of SEQ ID NO:2.

8. The cDNA molecule of claim 7 which encodes SEQ ID NO:2.

9. The cDNA molecule of claim 8 which comprises SEQ ID NO:1.

10. A cDNA molecule comprising at least 12 contiguous nucleotides of SEQ ID NO:1.

11. A cDNA molecule which is at least 85% identical to the nucleotide sequence shown in SEQ ID NO:1, wherein percent identity is determined using a Smith-Waterman homology search algorithm using an affine gap search with a gap open penalty of 12 and a gap extension penalty of 1.

12. An isolated and purified subgenomic polynucleotide comprising a nucleotide sequence which hybridizes to SEQ ID NO:1 after washing with 0.2X SSC

at 65 °C, wherein the nucleotide sequence encodes a huBUB3 protein having the amino acid sequence of SEQ ID NO:2.

13. A construct comprising:

a promoter; and

a polynucleotide segment encoding at least 8 contiguous amino acids of a huBUB3 protein as shown in SEQ ID NO:2, wherein the polynucleotide segment is located downstream from the promoter, wherein transcription of the polynucleotide segment initiates at the promoter.

14. A host cell comprising a construct which comprises:

a promoter and:

a polynucleotide segment encoding at least 8 contiguous amino acids of a huBUB3 protein having an amino acid sequence as shown in SEQ ID NO:2.

15. A recombinant host cell comprising a new transcription initiation unit, wherein the new transcription initiation unit comprises in 5' to 3' order:

(a) an exogenous regulatory sequence;

(b) an exogenous exon; and

(c) a splice donor site,

wherein the new transcription initiation unit is located upstream of a coding sequence of a *huBUB3* gene as shown in SEQ ID NO:1, wherein the exogenous regulatory sequence controls transcription of the coding sequence of the *huBUB3* gene.

16. A pair of single-stranded DNA primers, said set allowing synthesis of all or part of a *huBUB3* gene coding sequence.

17. The pair of claim 16 wherein the primers have restriction enzyme sites at each 5' end.

18. A nucleic acid probe complementary to a wild-type *huBUB3* gene as shown in SEQ ID NO: 1.

19. A method of diagnosing a neoplastic tissue of a human, comprising the step of:

detecting loss of a wild-type *huBUB3* gene or an expression product of the wild-type *huBUB3* gene from a tissue suspected of being neoplastic, wherein

the wild-type *huBUB3* gene has the coding sequence shown in SEQ ID NO:1, wherein the loss indicates neoplasia of the tissue.

20. The method of claim 19 wherein the expression product is an mRNA molecule.

21. The method of claim 19 wherein the expression product is a protein molecule.

22. The method of claim 19 wherein the loss of the wild-type *huBUB3* gene is detected by sequencing all or part of a *huBUB3* gene.

23. The method of claim 19 wherein the loss of the wild-type *huBUB3* gene is detected by amplification of *huBUB3* gene sequences and hybridization of the amplified *huBUB3* sequences to nucleic acid probes which are complementary to mutant *huBUB3* alleles.

24. The method of claim 19 wherein the loss of the wild-type *huBUB3* gene is detected by sequencing all or part of a *huBUB3* gene.

25. The method of claim 21 wherein the loss of the wild-type huBUB3 protein molecule is detected by detecting a loss of ability of a huBUB3 protein to complex with a BUB1 protein.

26. The method of claim 19 wherein detection of the loss of the wild-type *huBUB3* gene comprises screening for a point mutation.

27. The method of claim 26 wherein the point mutation is a missense mutation.

28. The method of claim 19 wherein detection of the loss of the wild-type *huBUB3* gene comprises screening for a frameshift mutation.

29. The method of claim 19 wherein the detection of the loss of the wild-type *huBUB3* gene comprises screening for a deletion mutation.

30. The method of claim 19 wherein the tissue suspected of being neoplastic is selected from the group consisting of lung, breast, brain, colorectal, bladder, prostate, liver, and stomach.

31. A method of identifying a neoplastic tissue of a human, comprising the step of:

comparing expression of a first *huBUB3* gene in a first tissue of a

human suspected of being neoplastic with expression of a second *huBUB3* gene in a second tissue of the human which is normal, wherein the second *huBUB3* gene has the coding sequence shown in SEQ ID NO:1, wherein decreased expression of the first *huBUB3* gene relative to the second *huBUB3* gene identifies the first tissue as being neoplastic.

32. A method to aid in the diagnosis or prognosis of neoplasia in a human, comprising the step of:

comparing a first *huBUB3* gene, mRNA, or protein in a first tissue of a human suspected of being neoplastic with a second *huBUB3* gene, mRNA, or protein in a second tissue of a human which is normal, wherein a difference between the first and second *huBUB3* genes, mRNAs, or proteins indicates the presence of neoplastic cells in the first tissue.

33. A method to aid in detecting a genetic predisposition to neoplasia in a human, comprising the step of:

comparing a *huBUB3* gene, mRNA, or protein in the fetal tissue of a human with a wild-type *huBUB3* gene, mRNA, or protein, wherein a difference between the *huBUB3* gene, mRNA, or protein in the fetal tissue of the human and the wild-type human *huBUB3* gene, mRNA, or protein indicates a genetic predisposition to neoplasia in the human.

34. A method of screening test compounds for the ability to interfere with the binding of a huBUB3 protein to a huBUB1 protein, comprising the steps of:

(a) contacting a test compound with at least a huBUB3-binding domain of a huBUB1 protein as shown in SEQ ID NO:4 and at least a huBUB1-binding domain of a huBUB3 protein as shown in SEQ ID NO:2, wherein the huBUB3-binding domain binds to the huBUB1-binding domain in the absence of the test compound; and

(b) determining the amount of the huBUB1-binding domain which is bound or unbound to the huBUB3-binding domain or determining the amount of the huBUB3-binding domain which is bound or unbound to the huBUB1-binding domain in the presence of the test compound, wherein a test compound which decreases the amount of bound huBUB1- or huBUB3-binding domains or which

increases the amount of unbound huBUB1- and huBUB3-binding domains is a potential inducer of mitosis or cell cycle progression.

35. The method of claim 34 wherein the huBUB1- and the huBUB3-binding domains are prebound prior to the step of contacting.

36. The method of claim 34 wherein the test compound is contacted with either of the huBUB1- or huBUB3-binding domains prior to the step of contacting.

37. A method of screening test compounds for the ability to interfere with the binding of a huBUB1 protein to a huBUB3 protein, comprising the steps of:

(a) contacting a cell with a test compound, wherein the cell comprises:

I) a first fusion protein comprising (1) at least a huBUB1-binding domain of a huBUB3 protein as shown in SEQ ID NO:2 and (2) either a DNA binding domain or a transcriptional activating domain;

ii) a second fusion protein comprising at least a huBUB3-binding domain of a huBUB1 protein as shown in SEQ ID NO:4, wherein the huBUB1-binding domain binds to the huBUB3-binding domain, wherein if the first fusion protein comprises a DNA binding domain, then the second fusion protein comprises a transcriptional activating domain, wherein if the first fusion protein comprises a transcriptional activating domain, then the second fusion protein comprises a DNA binding domain, wherein the interaction of the first and second fusion proteins reconstitutes a sequence-specific transcription activating factor; and

iii) a reporter gene comprising a DNA sequence to which the DNA binding domain specifically binds; and

(b) measuring the expression of the reporter gene, wherein a test compound which decreases the expression of the reporter gene is a potential inducer of mitosis or cell cycle progression.

38. A method of identifying compounds which interfere with the binding of a huBUB3 protein to a huBUB1 protein, comprising the steps of:

providing a cell which comprises three recombinant DNA constructs, wherein a first construct encodes a first polypeptide fused to a sequence-specific DNA-binding domain, wherein a second construct encodes a second polypeptide fused to a transcriptional activation domain, and wherein a third construct comprises

a reporter gene downstream from a DNA element which is recognized by the sequence-specific DNA-binding domain, wherein the first polypeptide comprises a huBUB1-binding domain of a huBUB3 protein as shown in SEQ ID NO:2 and the second polypeptide comprises a huBUB3-binding domain of a huBUB1 protein as shown in SEQ ID NO:4 or the first polypeptide comprises a huBUB3-binding domain of a huBUB1 protein as shown in SEQ ID NO:4 and the second polypeptide comprises a huBUB1-binding domain of a huBUB3 protein as shown in SEQ ID NO:2;

contacting the cell with a test compound; and

determining expression of the reporter gene in the presence of the test compound, wherein a test compound which decreases expression of the reporter gene is identified as a candidate therapeutic agent.

39. A cell which comprises three recombinant DNA constructs, wherein a first construct encodes a first polypeptide fused to a sequence-specific DNA-binding domain, wherein a second construct encodes a second polypeptide fused to a transcriptional activation domain, and wherein a third construct comprises a reporter gene downstream from a DNA element which is recognized by the sequence-specific DNA-binding domain, wherein the first polypeptide comprises a a huBUB1-binding domain of a huBUB3 protein as shown in SEQ ID NO:2 and the second polypeptide comprises a huBUB3-binding domain of a huBUB1 protein as shown in SEQ ID NO:4, or the first polypeptide comprises a huBUB3-binding domain of a huBUB1 protein as shown in SEQ ID NO:4 and the second polypeptide comprises a huBUB1-binding domain of a huBUB3 protein as shown in SEQ ID NO:2

40. A method of determining the quantity of huBUB1 which binds to huBUB3, or of huBUB3 which binds to huBUB1, comprising the steps of:

contacting a first protein and a second protein, wherein if the first protein is huBUB3 the the second protein is huBUB1 and if the first protein is huBUB1 the the second protein is huBUB3; and

determining the quantity of the first protein which is bound to the second protein.

41. A method for identifying compounds which decrease the kinase activity of a huBUB1-huBUB3 complex, comprising the steps of:

contacting a huBUB1-huBUB3 complex with a test compound; and

determining the kinase activity of the huBUB1-huBUB3 complex, wherein a compound which decreases kinase activity of the huBUB1-huBUB3 complex is identified as a candidate therapeutic agent.